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David de Graaf

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MORSE, BARNES-BROWN & PENDLETON, P.C.

ATTN: IP MANAGER

RESERVOIR PLACE

1601 TRAPELO ROAD, SUITE 205

WALTHAM, MA 02451

EXAMINER

STEELE, AMBER D

ART UNIT

PAPER NUMBER

1639

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 09/804,481	<b>Applicant(s)</b> GRAAF ET AL.	
	<b>Examiner</b> AMBER D. STEELE	<b>Art Unit</b> 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on October 20, 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 32-35,39,41-46 and 48 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 32-35,39,41-46 and 48 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Status of the Claims***

1. The amendment to the claims received on February 9, 2009 canceled claims 1-31, 36-38, 47, and 52-53 and amended claims 32, 39, 42, and 49.

The amendment to the claims received on October 20, 2009 amended claims 32, 39, 41, and 42, and canceled claims 40 and 49-51.

Claims 32-35, 39, 41-46, and 48 are currently pending and under consideration.

### ***Priority***

2. The present application claims benefit of U.S. provisional application 60/188,304 filed March 10, 2000.

### ***Sequence Compliance***

3. The present application is currently in compliance with the sequence rules.

### ***Invention as Claimed***

4. Independent claim 32: A recombinant vector comprising an isolated nucleotide sequence encoding an snRNA wherein the snRNA-encoding portion of said snRNA-encoding nucleotide sequence has been modified to contain a recognition site for a dual cleavage restriction enzyme capable of cleaving said nucleotide sequence once upstream of said recognition site and once downstream of said recognition site and excising from said vector a restriction fragment which includes said recognition site and variations thereof.

Independent claim 39: A recombinant vector comprising an isolated nucleotide sequence encoding an snRNA wherein the snRNA-encoding portion of said snRNA-encoding nucleotide sequence has been modified to contain a recognition site for restriction enzyme BaeI and

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variations thereof.

Independent claim 42: A recombinant vector comprising an isolated nucleotide sequence encoding an snRNA wherein the snRNA-encoding portion of said snRNA-encoding nucleotide sequence comprises an insertion cassette comprising a modification fragment comprising a nucleotide sequence complementary to a target and variations thereof.

5. The presently claimed invention contains process steps (i.e. “excising from said vector a restriction fragment which includes said recognition site” of present independent claim 32, “excises a double stranded restriction fragment with single stranded overhangs at each end and forms insertion sites comprising single stranded overhangs which are complementary to the single stranded overhangs of the restriction fragment” of present claim 41) and functional limitations (i.e. “capable of cleaving said nucleotide sequence once upstream of said recognition site and once downstream of said recognition site” of present independent claim 32). See MPEP § 2113 and § 2173.05(g). Only the structure required by the presently claimed invention will be provided patentable weight (i.e. recombinant vector comprising an isolated nucleotide sequence encoding a snRNA wherein the snRNA-encoding portion of said snRNA-encoding nucleotide sequence has been modified to contain a recognition site for a dual cleavage restriction enzyme).

### **New Objections**

#### ***Claim Objections***

6. Claims 32, 39, and 42 are objected to because of the following informalities: “an snRNA” should read “a snRNA” (see line 2 of each claim). Appropriate correction is required.

### **Withdrawn Rejections**

7. The rejection of claims 32-35, 39-46, and 48-51 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement regarding new matter is withdrawn in view of the claim amendments received on October 20, 2009 and in view of the response received on October 20, 2009 which specifically pointed out support for the claim amendments.

8. The rejection of claims 39, 42-46, and 48 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention regarding the indefinite nature of the claims is withdrawn in view of the claim amendments received on October 20, 2009.

### **Maintained Rejections**

#### ***Claim Rejections - 35 USC § 112***

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 32-35 and 41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. One of skill in the art would not be able to determine the scope of the presently claimed invention. For example, the presently claimed vector refers to an intermediate vector while process limitations are present regarding the production of a final product. Therefore, it is not clear from the present claims if the intermediate vector or the final vector is required by the claims. See section 5 above regarding the claimed invention.

***Arguments and Response***

11. Applicants' arguments directed to the rejection under 35 USC 112, second paragraph (indefinite), for claims 32-35 and 41 were considered but are not persuasive for the following reasons.

Applicants contend that all process limitations were deleted in the amendment received on October 20, 2009.

Applicants' arguments are not convincing since process limitations are still present in the claims. The presently claimed invention contains process steps (i.e. "excising from said vector a restriction fragment which includes said recognition site" of present independent claim 32, "excises a double stranded restriction fragment with single stranded overhangs at each end and forms insertion sites comprising single stranded overhangs which are complementary to the single stranded overhangs of the restriction fragment" of present claim 41).

***Claim Rejections - 35 USC § 103***

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. Claims 32-35, 39, 41-46, and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Noonberg et al. U.S. Patent 5,624,803 issued April 29, 1997; Halle et al. U.S. 6,303,308 (effective filing date of May 10, 1999); and Abounader et al., Design and Expression of Chimeric U1/Ribozyme Transgenes, *Methods in Molecular Biology*, 252: 209-219.

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For present claims 32-34, 39, 41-46, and 48, Noonberg et al. teach vectors comprising a U6 snRNA promoter, a stabilizing region from which a hairpin-forming sequence can be transcribed, a nucleotide sequence of interest (wherein the sequence was inserted via the incorporation of two restriction enzyme cleavage sites), and a termination sequence wherein the stabilizing region is a sequence encoding a U6 snRNA hairpin region and the termination sequence is a sequence encoding a U6 snRNA and U1 (please refer to the entire specification particularly columns 8, 12-16, 18, 20-21; Examples 3-4; claims 1-3, 5, 16, 21-22, 24, and 26). In addition, Noonberg et al. teach that any restriction endonuclease can be utilized as long as two cleavage sites are present; any snRNA promoter, stabilizing region, and termination sequence can be utilized; and the sequence of interest can be between 10 and 60 nucleotides in length (please refer to the entire specification particularly columns 15-16, 18). Furthermore, Noonberg et al. teach a mutant U6 gene comprising only the first 6 and last 10 base pairs (see Example 3; Kunkel et al., Transcription of a human U6 small nuclear RNA gene *in vivo* withstands deletion of intragenic sequences but not of an upstream TATATA box, Nucleic Acids Research, 17(18): 7371-7379).

However, Noonberg et al. does not teach BaeI.

For present claims 32, 39, 41, and 42, Halle et al. teach cloning vectors comprising BaeI (please refer to the entire specification particularly the abstract; columns 3 and 11; claims 1 and 13).

However, Noonberg et al. does not teach U1 snRNA modified with the first 11 nucleotides of the coding region.

For present claims 33-35 and 44-46, Abounader et al. teach a vector comprising a U1

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snRNA chimeric transgene wherein the U1 snRNA loops flank an insert (please refer to the entire reference particularly the abstract; Figure 1; sections 2.2, 3.2).

The claims would have been obvious because the substitution of one known element (i.e. U6 snRNA and restriction enzymes taught by Noonberg et al.) for another (i.e. U1 snRNA taught by Abounader et al. and BaeI taught by Halle et al.) would have yielded predictable results (i.e. expression of either U6 or U1, restriction enzyme cleavage) to one of ordinary skill in the art at the time of the invention. See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

### ***Arguments and Response***

14. Applicants' arguments directed to the rejection under 35 USC 103 (a) as being unpatentable over Noonberg et al., Halle et al., and Abounader et al. for claims 32-35, 39, 41-46, and 48 were considered but are not persuasive for the following reasons.

Applicants contend that Noonberg et al. does not teach vectors comprising a nucleotide sequence encoding snRNA.

Applicants' arguments are not convincing since the teachings of Noonberg et al., Halle et al., and Abounader et al. render the invention of the instant claims *prima facie* obvious.

Noonberg et al. teach the entire U6 snRNA gene, vectors comprising the U6 promoter, a stabilizing region which can be the first 25 nucleotides of human U6 snRNA, and a termination sequence which can be approximately 20 nucleotides of the 3' portion of human U6 snRNA (see the entire specification particularly Figure 4A-4C, 5A-5C, 6A-6B, 7A-7B, 8, 9A-9B, 15-17, 18A-18C, 19, 20B, 21, 22, 27A, 27B; columns 8-12, 14, 16, 20; Examples 3, 5). It is noted that



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the present claims do not require the full length snRNA and in fact require modification of the snRNA (see present independent claims 32, 39, and 42).

**New Rejections Necessitated by Amendment**

***Claim Rejections - 35 USC § 102***

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 32-34, 41-46, and 48 are rejected under 35 U.S.C. 102(b) as being anticipated by Noonberg et al. U.S. Patent 5,624,803 issued April 29, 1997.

For present claims 32-34, 41-46, and 48, Noonberg et al. teach vectors comprising a U6 snRNA promoter, a stabilizing region from which a hairpin-forming sequence can be transcribed, a nucleotide sequence of interest (wherein the sequence was inserted via the incorporation of restriction enzyme cleavage sites), and a termination sequence wherein the stabilizing region is a sequence encoding a U6 snRNA hairpin region and the termination sequence is a sequence encoding a U6 snRNA and U1 (please refer to the entire specification particularly columns 8, 12-16, 18, 20-21; Examples 3-4; claims 1-3, 5, 16, 21-22, 24, and 26). In addition, Noonberg et al. teach restriction endonucleases including XhoI and NsiI, that any restriction endonucleases can be utilized as long as two cleavage sites are present; any snRNA promoter, stabilizing region, and termination sequence can be utilized; and the sequence of interest can be between 10 and 60 nucleotides in length (please refer to the entire specification particularly columns 15-16, 18).

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Furthermore, Noonberg et al. teach a mutant U6 gene comprising only the first 6 and last 10 base pairs (see Example 3).

Therefore, the presently claimed invention is anticipated by the teachings of Noonberg et al.

### ***Conclusion***

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

### ***Future Communications***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AMBER D. STEELE whose telephone number is (571)272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amber D. Steele/  
Primary Examiner, Art Unit 1639